REMARKS

The Specification has been amended to update the status of U.S. Application Ser. Nos. 10/695,536 and 10/230,133, and to indicate the relationship of the instant application to U.S. Serial No. 10/695,536. Applicant has further amended the Specification to provide proper antecedent basis for the term "enzyme-linked immunosorbent assay" and to correct the misspelling of tachykinin(s), and has reviewed for and corrected other minor errors, all as requested by the Examiner.

Claims 2 and 7-18 have been canceled, without prejudice. The cancellation of these claims obviates the rejection of these claims.

Independent Claims 1 and 19 have been amended in order to clarify the method of the invention and correct minor typographical errors, and further, to limit the claims to methods for assessing or monitoring progress in treatment of preeclampsia, respectively. Claims 1 and 19 have been further amended to claim methods comprising measurement of peptides, wherein the peptides are limited to peptides selected from the group consisting of the amino acid sequences of SEQ ID NO:2, SEQ ID NO: 1, and SEQ ID NO: 4. It is believed that none of these amendments constitute new matter and their entry is requested.

Claims 1-6 and 19 include all essential method steps.

The Examiner has rejected claims 1-19 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps. Applicant respectfully traverses this rejection as to the pending claims.

Claim 1 makes explicit that which is described in the Specification, namely that a predisposition to preeclampsia can be assessed by comparing the level of peptide in a sample of body fluid of the individual being tested to a standard representing normal levels of peptide,

whereby a significantly lower level of the peptide in the sample of body fluid is indicative of predisposition of the individual to preeclampsia. Claim 1 thus provides all essential steps of the claimed method. Likewise, Claim 19 includes the essential steps described in the Specification for monitoring progress in treatment of preeclampsia. The techniques that can be employed in measuring peptide levels, while not previously practiced with the methods of the invention, are otherwise known in the art as having been practiced in the detection of other peptides/proteins. Thus, Applicant urges that no further recitations are necessary, and that one of ordinary skill in the art could determine from a reading of the instant Specification all essential steps in measuring the level of peptide. Although a preferred embodiment of the method of the instant claims employs immunochemical procedures and standards, any art recognized method and appropriate standard for measuring and comparing the level of peptide may be used. See paragraphs [0034], [0057], [0088], and [0148]. To add specific steps would force Applicant to a preferred embodiment, when it is axiomatic that claims need not be limited to a preferred embodiment. Accordingly, withdrawal of the rejection of the pending claims under 35 U.S.C. 112, second paragraph, is respectfully requested.

Claims 1-6 and 19 are fully enabled.

The Examiner has rejected claims 1-6 and 13-19 under 35 U.S.C. 112, first paragraph, as not providing enablement commensurate in scope with the claims. Specifically, as basis for this rejection, Examiner comments that Applicant has not correlated levels of tachykinin peptides with level of bound magnesium as measured by atomic absorption spectrophotometry. Applicant respectfully traverses the Examiner's rejection.

The Specification teaches that the levels of the peptides of the instant application correlate with the magnesium binding defect through its teaching that the administration of the disclosed

peptides correct the magnesium binding defect. The Specification further reports the discovery of an association of preeclampsia with the magnesium binding defect, which discovery has yielded the claimed diagnostic methodology for preeclampsia. Specifically, the specification discloses:

"...the substances in normal human and rat plasmas which can ameliorate or correct the magnesium binding defect in erythrocyte membranes are the pentapeptide, Phe-Phe-Gly-Leu-Met-NH_2 (SEQ ID NO:1) and the tetrapeptide, Phe-Gly-Leu-Met-NH_2 (SEQ ID NO:2) (Wells and Agrawal, In press; U.S. Pat. No. 6,372,440)." (Paragraph [0047])

"Furthermore, it has been discovered that the intravenous administration of the tetrapeptide of SEQ ID NO:2 to the salt-sensitive SS/Jr rat not only corrects the magnesium binding defect in erythrocytes of the SS/Jr rat, but also reduced its systolic blood pressure from an elevated value of 210 mm Hg to the control value, which is the blood pressure of the SR/Jr rats (Wells and Agrawal, In press). Thus, the correlation between the levels of the peptides of the present invention in body fluids and abnormal physiological states associated with MgBD is established by the discoveries reported herein." (Paragraph [0047])

The present claims are directed to a method of assessing a predisposition of an individual to preeclampsia. Specifically, the method involves measuring the level of peptide in a sample of body fluid of the individual, and comparing the level to a standard. (See paragraph [0034].) The peptide measured in the method of the invention is selected from the group consisting of the amino acid sequence of SEQ ID NO:2 (the "tetrapeptide"), and the amino acid sequences of SEQ ID NO: 1, and SEQ ID NO: 4 (the "pentapeptides"). Applicant emphases that it is the level of the tetrapeptide and/or pentapeptides, not the level of substance P or other tachykinins, that has been discovered to inversely correlate with the presence of the magnesium binding defect ([0018]).

The level of the tetrapeptide and/or pentapeptides therefore also inversely correlate with levels of magnesium bound to the plasma membranes of somatic cells. (See paragraphs [0026] and [0033].) Specifically, the discoveries reported in the instant application teach that the tetrapeptide and pentapeptides are substances which promote binding of magnesium *in vivo*, and which therefore ameliorate or correct the magnesium binding defect. (See paragraph [0047] and Example 2.) The specification further teaches that the tetrapeptide and pentapeptides can promote the *in vitro* binding of magnesium ions to the plasma membranes of magnesium deficient erythrocytes. (See paragraph [0111] and Example 7.) It is the levels of these tetrapeptide and pentapeptide promoters that are measured in the method of the claims under examination, not the level of tachykinins, such as substance P or neurokinins A or B. Applicant notes in this regard that the tetrapeptide and pentapeptide are significantly more active than Substance P in promoting binding of magnesium of magnesium deficient erythrocytes. (See paragraph [0143].)

The correlation between the levels of tetrapeptide and/or pentapeptides and the presence of and predisposition to preeclampsia is established by the discoveries reported in the Specification. Thus, Applicant submits that the Specification would enable one of ordinary skill in the art to practice the full breadth of the claims, without undue experimentation, and therefore requests withdrawal of the rejection under 35 U.S.C. 112, first paragraph.

Claims 1-6 and 19 are not anticipated or made obvious by the cited references.

The Examiner has rejected claims 1, 7-11 and 19 under 35 U.S.C.102(b), as being anticipated by Faulhaber et al. or Mori et al., and further as unpatentable under 35 U.S.C. 103 over Faulhaber et al. or Mori et al., in view of Couraud et al. The rejections of claims 7-11 are obviated by the cancellation of these claims. Claims 1-6 and 19 have been amended to a method

for assessing the predisposition of an individual to preeclampsia and method for monitoring progress in treatment of preeclampsia, respectively. Neither Faulhaber et al. or Mori et al. teach or suggest, and therefore can not anticipate or make obvious, the methods of the present claims. Accordingly, withdrawal of the rejections under 35 U.S.C. 120(b) and 23 U.S.C. 103 is respectfully requested.

Claims 1-6 and 19 are patentably distinct from the claims of U.S. Patent No. 6,372,440.

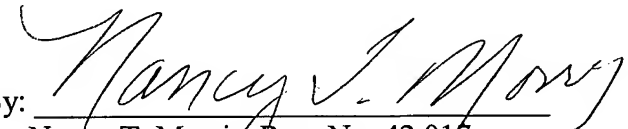
The Examiner has rejected Claims 1-19 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,372,440 (the "'440 Patent"). Applicant respectfully traverses this rejection.

The claims of the '440 Patent are directed to a method for detecting the magnesium binding defect in blood plasma by measuring the levels of peptides and comparing same to a standard. The portions of the '440 Patent specification that support the claims disclose the association of salt-sensitive hypertension and type 2 diabetes mellitus with presence of the magnesium binding defect. Claims 1-6 and 19 of the instant application are directed to a method of assessing a predisposition of an individual to preeclampsia and a method of monitoring progress in treatment of preeclampsia. The discovery of an association between preeclampsia reported in the present application, and not known in the prior art, makes possible the novel diagnostic methods for preeclampsia of the instant claims. No correlation between preeclampsia and the magnesium binding defect is disclosed or suggested in the '440 Patent specification. Nor does the '440 Patent teach or suggest a method for assessing a predisposition or monitoring progress in treatment of preeclampsia. Thus, without the teachings of the present application, one of skill in the art would not conclude that the instant claims are obvious variations of claims 1-7 of the '440 Patent.

In summary, the claims of the instant application are not obvious variations or anticipated by the claims of the '440 Patent, and are therefore patentably distinct from the claims of the '440 Patent. Accordingly, withdrawal of these rejections is respectfully requested.

In view of the foregoing amendments and remarks, it submitted that the claims remaining for active consideration in this application are free of the cited art and in condition for allowance. Accordingly, favorable action at an early date will be appreciated. If the examiner is of the view that any issue remains unresolved, it is respectfully suggested that Applicant's undersigned attorney may be contacted by telephone at the number set forth below.

Respectfully submitted,

By: 

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